REMARKS

The Office Action dated February 19, 2004 presents the examination of claims 1-14. Claims 1-14 are canceled. Claims 15-30 are added. Support for the claims is found in the specification. Particular support is listed in the table below. No new matter is inserted into the application.

Claim Number	Support in Substitute Specification
Independent claim 15, and dependent claims 16-17	Page 18, line 23 to page 19, line 10; Page 32, line 6 to page 33, line 22; Example 10
Independent claim 18, and dependent claims 19-22	Page 32, line 6 to page 33, line 22; Page 41, line 23 to page 42, line 5; Examples 8 and 11
Independent claim 23, and dependent claims 24-26	Page 27, lines 5-20; Page 20, line 4 to page 21, line 11
Independent claim 27, and dependent claims 28-29	Page 21, line 12 to page 27, line 4; Example 5
Independent claim 30	Page 26, line 19 to page 27, line 4

Specification

The Examiner requires correction of all grammatical, idiomatic, and spelling errors in the specification. Attached hereto is a substitute specification, excluding the claims, in full compliance with 37 C.F.R. § 1.125(b). In accordance with 37 C.F.R.

§ 1.125(c), the substitute specification is submitted in clean form without markings. A marked-up copy of the substitute specification showing all changes made to the specification of record is also submitted herewith. Any text added is underlined, and any text deleted is shown by a strike-through of the deleted text. The substitute specification does not include any new matter. Entry thereof is respectfully requested.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 9 and 11-14

The Examiner rejects claims 9 and 11-14 under 35 U.S.C. § 112, first paragraph, for an alleged lack of written description and enablement. Claims 9 and 11-14 are canceled, thus rendering the rejection thereof moot. Applicants respectfully traverse the rejection if applied to any of new claims 15-30. Consideration of the claims and withdrawal of the instant rejection are respectfully requested.

Former claims 9 and 11-14 recite Accession No. FERM BP-7295 and Accession No. FERM BP-7296. The Examiner asserts that the specification does not provide evidence that the deposits are either: (1) known and readily available to the public; (2) reproducible from the description in the specification; or (3)

deposited in an acceptable public repository.

New claims 29 and 30 recite an antibody produced by a hybridoma cell line deposited as Accession No. FERM BP-7295 or Accession No. FERM BP-7296, and a hybridoma cell line deposited as Accession No. FERM BP-7295 or Accession No. FERM BP-7296, respectively.

FERM BP-7295 and FERM BP-7296 are deposited at Bio Engineering and Industrial Technology Laboratory, Institute of Industrial Science and Technology at 1-3, Higashi 1-chome, Tsukuba-shi, Ibaragi-ken, Japan. Bio Engineering and Industrial Technology Laboratory is an International Depository Authority (IDA) established under the Budapest Treaty, as shown in the English portion of the Declaration of Deposit. A copy of the Declaration of Deposit with the English portion highlighted is attached hereto for the Examiner's convenience.

Applicants' representative hereby states that the hybridoma cell lines of Accession No. FERM BP-7295 and Accession No. FERM BP-7296 are deposited under the Budapest Treaty, that the hybridoma cell lines will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, and that the hybridoma cell lines will be replaced should they ever become non-viable.

For all of the above reasons, the criteria for deposit of biological material set forth in 37 C.F.R. §§ 1.801-1.809 are fully satisfied. Withdrawal of the instant rejection is therefore respectfully requested.

Claims 1-4 and 14

The Examiner also rejects claims 1-4 and 14 under 35 U.S.C. § 112, first paragraph for allegedly lacking written description in the specification. Claims 1-4 and 14 are canceled, thus rendering the rejection thereof moot. Applicants respectfully traverse the rejection if applied to any of new claims 15-30. Consideration of the claims and withdrawal of the instant rejection are respectfully requested.

The Examiner alleges that the specification does not disclose any direct method for measuring low molecular weight soluble CD14 proteins. The Examiner asserts that, instead, the only immunological method disclosed is that of separately measuring the total amount of soluble CD14 proteins and the total amount of high molecular weight CD14 proteins, and then subtracting the total amount of molecular weight CD14 proteins from the total amount of soluble CD14 proteins to arrive at the amount of low molecular weight soluble CD14 proteins. Applicants respectfully disagree.

Low versus high molecular weight soluble CD14 proteins

First, Applicants wish to clarify the difference between low molecular weight soluble CD14 proteins and high molecular weight soluble CD14 proteins. The following table summarizes differences between the two types of proteins.

	Low molecular weight soluble CD14 proteins	**High molecular weight soluble CD14 proteins**	**Support in the substitute specification**
1. Amino acid sequence	42 or more amino acids are deleted from the C-terminus	Full length, or 41 or less amino acids are deleted from the C-terminus	Page 18, line 3 to page 19, line 10
2. Antibody binding	Does not bind to F1025-3-1	Binds to F1025-3-1	Examples 10 and 12
3. Molecular weight	Mainly 36 kDa	Mainly 55 kDa and 49 kDa	Page 19, line 8, and page 18, lines 19-21

As noted on page 18 of the substitute specification, human full length CD14 protein consists of 356 amino acid residues described in SEQ ID NO: 1. Any protein derived from the full length sequence which has 41 or less amino acids deleted from the C-terminus is considered a "high molecular weight soluble CD14 protein." On the other hand, any protein derived from the full length sequence which has 42 or more amino acids deleted from the C-terminus is considered a "low molecular weight soluble CD14 protein."

Given the above, it is clear to the skilled artisan that "low molecular weight soluble CD14 proteins" are clearly different from "high molecular weight soluble CD14 proteins" in amino acid sequence, ability to bind to certain antibodies, as well as in molecular weight.

The present invention

One embodiment of the present invention provides for a method for diagnosing sepsis. Specifically, new claim 15 is directed to a method for diagnosing sepsis by measuring the amount of low molecular weight soluble CD14 proteins having an amino acid sequence which has 42 or more amino acids from the C-terminus thereof deleted (when compared to the human full length soluble CD14 protein) in a body fluid, and comparing the measured value to a standard value of normal persons or patients. This method is based on the new finding by the present Inventors that a higher amount of low molecular weight soluble CD14 proteins is detected in the body fluid of patients suffering from sepsis than in the normal population.

Support for this method is found in the specification. In addition to the method for measuring of low molecular weight soluble CD14 proteins by immunological subtraction as described in Example

11 (and pointed out by the Examiner), the specification describes several other methods for measuring low molecular weight soluble CD14 proteins separately.

For example, as disclosed on page 32, line 8 *et seq.*, the method for measuring the low molecular weight soluble CD14 proteins is not particularly limited, and "may include a method of extracting soluble CD14 proteins from the body fluid, removing a high molecular soluble CD14 protein from the extract and measuring the amount of protein in the resulting liquid, a method of isolating soluble CD14 proteins in the body fluid by electrophoresis, HPLC, MS (mass spectrum) or the like and quantitatively determining the low molecular soluble CD14 protein, and the like."

Further, in Example 10 of the specification, the detection of low molecular weight soluble CD14 proteins by Western blotting is described. The electrophoretogram is shown in Fig. 6. Electrophoresis is a practical tool known to the skilled artisan at the time the present application was filed. Using the results of electrophoresis to measure the amount of low molecular weight soluble CD14 proteins is therefore well within the technical ability of the skilled artisan.

For example, Stelter et al. (*Eur. J. Biochem.*, Vol. 236:457, 1996) describes a method for measuring the amount of CD14 isoforms

by densitometric scanning. Specifically, sCD14 isoforms were purified by affinity chromatography, separated on SDS/PAGE, and detected by Western blotting (see Fig. 2). The relative values of the sCD14 isoforms are shown in Table 2. Moreover, in Landmann et al. (*J. Inf. Dis.*, 171:639, 1995), the amount of sCD14 proteins is measured by the signal obtained from the electrophoresis of sCD14 (see Fig. 3).

Thus, it is clear from the above that the results of electrophoresis can be used to measure the amount of protein, and that such technical knowledge was common to a person skilled in the art at the time the present application was filed. However, the present invention provides the information for the first time that there is a higher amount of low molecular weight soluble CD14 proteins in the body fluid of patients suffering from sepsis than in the normal population. Therefore, regardless of the method used to actually measure the proteins (since it is not particularly limited), the present invention provides for the first time a method of diagnosing sepsis.

Another embodiment of the present invention is a method for determining the amount of low molecular weight soluble CD14 proteins by the subtraction method. Specifically, new claim 18 is directed to a method for measuring low molecular weight soluble CD14

proteins having an amino acid sequence with 42 or more amino acids deleted from the C-terminus (when compared to human full length soluble CD14 proteins) in a body fluid. The steps of said method include: (A) measuring immunologically the total amount of soluble CD14 proteins in a body fluid; (B) measuring immunologically the amount of high molecular weight soluble CD14 proteins in the body fluid (which are human full length soluble CD14 protein and soluble CD14 proteins having an amino acid sequence with 41 or less amino acids deleted from the C-terminus of the amino acid sequence when compared to the human full length soluble CD14 protein); and subtracting the amount of high molecular weight soluble CD14 proteins from the total amount of soluble CD14 proteins.

This method is supported by Example 11 of the specification. Therefore, as acknowledged by the Examiner in the outstanding Office Action, this method is described and enabled by the specification.

For all of the above reasons, Applicants respectfully submit that the pending claims fully comply with 35 U.S.C. § 112, first paragraph. Withdrawal of the instant rejection is therefore respectfully requested.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejects claims 1-14 under 35 U.S.C. § 112, second paragraph for allegedly being indefinite. Claims 1-14 are canceled, thus rendering the rejection thereof moot. Applicants respectfully traverse the rejection if applied to any of new claims 15-30. Consideration of the claims and withdrawal of the instant rejection are respectfully requested.

"Low molecular" and "High molecular"

The Examiner asserts that the terms "low molecular" and "high molecular" are indefinite because "the specification does not provide a standard for ascertaining the requisite degree of 'molecular.'" The new claims do not recite "low molecular" or "high molecular" solely. Instead, the new claims recite "low molecular weight soluble CD14 proteins" and/or "high molecular weight soluble CD14 proteins." Further, the low molecular weight soluble CD14 proteins are defined in the claims as those having 42 or more amino acids deleted from the C-terminus of the CD14 amino acid sequence, whereas the high molecular weight soluble CD14 proteins are defined as either having the full-length CD14 amino acid sequence or 41 or less amino acids deleted from the C-terminal end. As noted above, support for this distinction is found on page

18, line 3 to page 19, line 10 of the substitute specification. As such, the instant rejection is overcome.

Method claims

The Examiner points out several former claims which allegedly did not set forth positive method steps. Applicants respectfully submit that all of the new method claims recite active, positive steps of the method, and conclude with a step relating back to the desired result set forth in the preamble. Support for new method claim 18, for example, is found on page 33, line 5 to page 34, line 20 of the substitute specification, as well as in Example 11. Support for new method claim 23 is found on page 20, line 4 to page 21, line 11, and on page 27, lines 5-16 of the substitute specification. As such, the instant rejection is overcome.

Other minor deficiencies

The Examiner also points out other minor deficiencies in the former claims, such as the lack of proper antecedent bases for the recited subject matter. Applicants respectfully submit that all of the newly pending claims are free of such minor deficiencies.

Based on the above, Applicants respectfully submit that the pending claims particularly point out and distinctly claim the subject matter which is the present invention. Withdrawal of the

instant rejection is therefore respectfully requested.

Rejection under 35 U.S.C. § 101

Claim 13

The Examiner rejects claim 13 under 35 U.S.C. § 101. Claim 13 is canceled thus rendering the rejection moot.

Claims 5-8 and 10

The Examiner also rejects claims 5-8 and 10 under 35 U.S.C. § 101 for allegedly being directed to non-statutory subject matter. Claims 5-8 and 10 are canceled thus rendering the rejection moot. Applicants respectfully traverse the rejection if applied to new claims 15-30. Consideration of the claims and withdrawal of the instant rejection are respectfully requested.

Claims 27 and 28 recite an isolated antibody. As such, the claims are directed to statutory subject matter. Withdrawal of the instant rejection is therefore respectfully requested.

Rejections under 35 U.S.C. § 102

Stelter et al.

The Examiner rejects claims 1, 2, 4, 5, 10, 13, and 14 under 35 U.S.C. § 102(b) for allegedly being anticipated by Stelter et

al. (*Eur. J. Biochem.*, 236:457 (1996)). Claims 1, 2, 4, 5, 10, 13, and 14 are canceled thus rendering the rejection moot. Applicants respectfully traverse the rejection if applied to new claims 15-30. Consideration of the claims and withdrawal of the instant rejection are respectfully requested.

Claim 15

As discussed in detail above, new claim 15 is directed to a method for diagnosing sepsis. Stelter et al. fails to disclose a method for diagnosing sepsis. Further, Stelter et al. fails to disclose that a higher amount of low molecular weight soluble CD14 proteins is detected in the body fluid of patients suffering from sepsis than in the normal population. For these reasons, Stelter et al. fails to disclose the embodiment of the present invention recited in claim 15 and claims dependent thereon.

Claim 18

As discussed in detail above, new claim 18 is directed to a method for measuring low molecular weight soluble CD14 proteins having an amino acid sequence with 42 or more amino acids deleted from the C-terminus (when compared to human full length soluble CD14 proteins) in a body fluid. The Examiner asserts that Stelter et al. teaches the use of antibodies to determine the relative

amounts of high and low molecular weight CD14 proteins in samples, as well as purified sCD14 which comprises the sequence of the polypeptide as claimed. Applicants respectfully submit that Stelter et al. fails to anticipate claim 18.

The serum-derived sCD14 proteins described by Stelter et al. have molecular weights of 53 kDa, 50 kDa, 46 kDa and 43 kDa (see Table 2). Furthermore, when the 53 kDa sCD14 protein and the 50 kDa sCD14 protein are subjected to the enzymatic deglycosylation, their derivative forms are a 46 kDa sCD14 protein and a 43 kDa sCD14 protein, respectively (see Fig. 3).

Applicants acknowledge that the 53 kDa sCD14 protein and 50 kDa sCD14 protein described by Stelter et al. fall within the definition of a "high molecular weight soluble CD14 protein" used in the instant specification. The 46 kDa sCD14 and 43 kDa sCD14 proteins also have the same sequence (other than a difference in the sugar chain) described as that of a "high molecular weight soluble CD14 protein" of the present invention.

However, Stelter et al. fails entirely to disclose or suggest a low molecular weight soluble CD14 protein as defined in the present invention. Furthermore, contrary to the Examiner's assertions, there is no disclosure or suggestion in Stelter et al. of how to measure the amount of these low molecular weight soluble

CD14 proteins in a sample.

As noted above, claim 18 recites that the low molecular weight soluble CD14 proteins have an amino acid sequence wherein 42 or more amino acids are deleted from the C-terminus of the human full length soluble CD14 protein. The molecular weight of such proteins is mainly 36 kDa. Stelter et al. does not describe any such low molecular weight soluble CD14 proteins. Indeed, the Examiner points to Table 2 as describing both high and low molecular weight soluble CD14 proteins. However, the molecular weights of the Stelter et al. proteins described in Table 2 are 43, 46, 50 and 53 kDa. As described immediately above, all of these proteins fall within the definition of "high molecular weight soluble CD14 proteins" used in the instant specification.

Claims 19-20

Additionally, the differences between Stelter et al. and the present invention is made even more distinct in claim 19, which defines the antibody used for measuring (the antibody which binds to amino acid positions 316-328 of the CD14 sequence), and in claim 20, which defines the use of the sandwich method.

The antibody used by Stelter et al. for Western blotting is an anti-CD14 polyclonal antibody. A polyclonal antibody would

presumably bind to both high molecular weight soluble CD14 proteins and low molecular weight soluble CD14 proteins. Therefore, it would be impossible to selectively measure either one of a high molecular weight soluble CD14 protein or a low molecular weight soluble CD14 protein using such an antibody.

On the contrary, claim 19 provides for a method for measuring low molecular weight soluble CD14 proteins by measuring only the amount of high molecular weight soluble CD14 proteins through the specific binding of the high molecular weight soluble CD14 protein to an antibody which selectively binds to positions 316 to 328 of the CD14 amino acid sequence, and subtracting the measured amount of high molecular weight soluble CD14 proteins from the total amount of soluble CD14 proteins. Since Stelter et al. fails to disclose or suggest the use of such an antibody, Stelter et al. fails to anticipate claim 19.

Claim 20 relates to a method for the measurement of low molecular weight soluble CD14 proteins by measuring only the amount of high molecular weight soluble CD14 proteins by the sandwich method using the antibody described above, and subtracting the measured amount of high molecular weight soluble CD14 proteins from the total amount of soluble CD14 proteins.

Again, Stelter et al. fails to disclose such an antibody and

further fails to disclose or suggest the use of such an antibody in a sandwich method for the method of measuring low molecular weight soluble CD14 proteins. Therefore, Stelter et al. fails to anticipate the subject matter of claim 20.

Claim 23

Claim 23 is directed to a method for measuring high molecular weight soluble CD14 proteins by reacting body fluid to anti-CD14 antibody which specifically binds to positions 316 to 356 of SEQ ID NO: 1. On the contrary, the antibody used for Western blotting by Stelter et al. is an anti-CD14 polyclonal antibody, which as discussed above would most likely non-selectively bind to both high and low molecular weight soluble CD14 proteins. Therefore, it would be impossible to selectively measure either one of the high molecular weight soluble CD14 protein or the low molecular weight soluble CD14 protein using the method disclosed by Stelter et al. The use of a selectively binding antibody such as that recited in the method of claim 23 is neither described nor suggested by Stelter et al. Thus, Stelter et al. fails to anticipate claim 23.

Claim 27

Finally, claim 27 recites an isolated antibody prepared by immunizing a mammal with a peptide having 6 to 41 consecutive amino

acids from positions 316 to 356 of SEQ ID NO: 1. In Stelter et al., although there is a description of an anti-CD14 antibody (antibody against native CD14), there is no description of an antibody prepared by immunizing a mammal with a polypeptide comprising 6 to 41 consecutive amino acids from positions 316 to 356 of SEQ ID NO:1 as an antigen. As such, Stelter et al. fails to anticipate claim 27.

In conclusion, it is clear that Stelter et al. fails to anticipate the newly pending claims. Withdrawal of the instant rejection is therefore respectfully requested.

Landmann et al.

The Examiner rejects claims 1, 4, 5, 10, and 13 under 35 U.S.C. § 102(b) for allegedly being anticipated by Landmann et al. (*J. Inf. Dis.*, 171:639 (1995)). Claims 1, 4, 5, 10, and 13 are canceled thus rendering the rejection moot. Applicants respectfully traverse the rejection if applied to new claims 15-30. Consideration of the claims and withdrawal of the instant rejection are respectfully requested.

Claim 15

As discussed in detail above, new claim 15 is directed to a method for diagnosing sepsis. Landmann et al. compares the

presence of two isoforms of sCD14 proteins (49 kDa and 55 kDa) in the blood sera of normal people, paroxysmal nocturnal hemoglobinuria patients, and sepsis patients. Landmann et al. discusses a correlation between increased sCD14 concentration in septic shock, which is also discussed in the "Background Art" section of the instant specification (see, e.g., page 5 of the substitute specification). Landmann et al. finds that sera from patients with gram-negative septic shock and controls had the 55 kDa sCD14 isoform but not the 49 kDa isoform, whereas sera from healthy volunteers contained either form (see, page 643, right column, final paragraph to page 644, left column, first paragraph).

Nevertheless, these 49 and 55 kDa isoforms fall within the definition of a high molecular weight soluble CD14 protein as used in the instant specification. See, for example, page 18, lines 19-21 of the substitute specification, wherein it is disclosed that two examples of high molecular weight soluble CD14 protein are a 55 kDa protein and a 49 kDa protein. Therefore, although Landmann et al. discusses the amount of high molecular weight soluble CD14 proteins in normal people, paroxysmal nocturnal hemoglobinuria patients, and sepsis patients, Landmann et al. fails to provide any description of low molecular weight soluble CD14 proteins as defined in the instant claims. Furthermore, there is no disclosure

or suggestion of a method for diagnosing sepsis via measuring low molecular weight soluble CD14 proteins.

For these reasons, Landmann et al. fails to anticipate the present invention as recited in claim 15.

Claim 23

Claim 23 is directed to a method for measuring high molecular weight soluble CD14 proteins by reacting body fluid to anti-CD14 antibody which specifically binds to positions 316 to 356 of SEQ ID NO: 1.

In contrast, the antibodies used in Western blotting in Landmann et al. are the 3C10 antibody and the anti-CD14 polyclonal antibody. As evidenced by WO 96/20957, the 3C10 antibody selectively binds to amino acid positions 7-14 of the CD14 amino acid sequence. Further, as discussed above, the anti-CD14 polyclonal antibody is non-specific and would therefore bind both a high molecular weight soluble CD14 protein and a low molecular weight soluble CD14 protein. Thus, given the antibodies utilized by Landmann et al., it would be impossible to selectively measure high molecular weight soluble CD14 proteins.

The use of a selectively binding antibody such as that recited in the method of claim 23 is neither described nor suggested by

Landmann et al. Thus, Landmann et al. fails to anticipate claim 23.

Claim 27

Finally, claim 27 recites an isolated antibody prepared by immunizing a mammal with a peptide having 6 to 41 consecutive amino acids from positions 316 to 356 of SEQ ID NO: 1. In Landmann et al., although there is a description of an anti-CD14 antibody (antibody against native CD14), there is no description of an antibody prepared by immunizing a mammal with a polypeptide comprising 6 to 41 consecutive amino acids from positions 316 to 356 of SEQ ID NO: 1 as an antigen. As such, Landmann et al. fails to anticipate claim 27.

In conclusion, it is clear that Landmann et al. fails to anticipate the newly pending claims. Withdrawal of the instant rejection is therefore respectfully requested.

Rejection under 35 U.S.C. §§ 102/103

The Examiner rejects claims 5-8 and 11 under 35 U.S.C. § 102(b) for allegedly being anticipated by, or in the alternative under 35 U.S.C. § 103(a) for allegedly being obvious over, Leturcq '025 (WO 94/28025). Claims 5-8 and 11 are canceled thus rendering the rejection moot. Applicants respectfully traverse the rejection if

applied to new claims 15-30. Consideration of the claims and withdrawal of the instant rejection are respectfully requested.

The Examiner asserts that the antibodies of Leturcq '025 are the same antibodies of the present invention, absent proof to the contrary. Applicants respectfully submit that the anti-CD14 antibody (antibody against a recombinant CD14) disclosed by Leturcq et al. is different from the antibody of the present invention.

Specifically, the present invention provides for an antibody prepared by immunizing a mammal with a polypeptide comprising 6 to 41 consecutive amino acids from amino acid positions 316 to 356 of SEQ ID NO: 1 as an antigen. There is no description of such an antibody in Leturcq et al.

In fact, an antibody produced by immunization with a full length sCD14 amino acid sequence (as disclosed by Leturcq et al.) only has the possibility to become specific for those epitopes exposed on the surface of the CD14 protein. Whether the amino acids of the 316 to 356 amino acid region form an epitope or not, as well as whether an antibody which binds to only this amino acid region exists or not, is unpredictable and therefore is not obvious. In contrast, the antibody recited in claim 27 only binds to an amino acid sequence wherein the specific amino acid sequence (i.e., positions 316 to 356) is present.

The Examiner is reminded that in order to establish inherency, "the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill in the art. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.'" In re Robertson, 169 F.3d 743, 745 (Fed. Cir. 1999) (citations omitted).

For these reasons, Laturcq et al. fails to anticipate or render obvious the present invention. Withdrawal of the instant rejection is therefore respectfully requested.

Conclusion

Applicants respectfully submit that the above remarks and/or amendments fully address and overcome the outstanding rejections and objections. For the foregoing reasons, Applicants respectfully request the Examiner to withdraw all of the outstanding rejections and objections, and to issue a Notice of Allowance indicating the patentability of claims 15-30. Early and favorable action of the merits of the present application is thereby respectfully requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Kristi L. Rupert, Ph.D. (Reg. No. 45,702) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), the Applicants hereby petition for an extension of three (3) months to August 19, 2004, in which to file a reply to the Office Action. The required fee of $950.00 is enclosed herewith.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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Attachment(s): Substitute specification (clean copy and marked-up copy);
Declaration of Deposit (copy)